

Primary Adenocarcinoma of an Ileostomy in Crohn's Disease

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ABSTRACT

Although Crohn's disease has been associated with an increased risk of small bowel adenocarcinoma, primary adenocarcinoma arising from an ileostomy is a complication that has been rarely documented in Crohn's disease. Chronic small bowel inflammation may lead to development of malignancy through the dysplasia-carcinoma sequence. We report a case of a 61-year-old woman with Crohn's ileocolitis diagnosed with a primary adenocarcinoma at the ileostomy with metastases to the liver 47 years after proctocolectomy, and review the literature.

INTRODUCTION

Although the small intestine has the lowest incidence of malignancy in the gastrointestinal tract, the overall risk of small bowel carcinoma in Crohn's disease (CD) patients has been found to be 60-fold greater than the general population.^{1,2} Primary adenocarcinoma of an ileostomy has been described predominantly in ulcerative colitis and reported in familial adenomatous polyposis and Hirschsprung's disease but reported only rarely in the literature as a complication of CD.^{3,4}

CASE REPORT

A 61-year-old woman was diagnosed with ulcerative colitis at age 14 and underwent total proctocolectomy with Brooke ileostomy. She developed abdominal pain at age 34 and was found to have Crohn's enteritis with small bowel strictures on ileoscopy. She was maintained in remission on oral azathioprine 100 mg daily and oral mesalazine 4 g daily. Forty-seven years after her initial diagnosis, she noted stoma retraction and pain with expanding peristomal ulceration. She experienced no improvement with topical silver nitrate or oral steroids initiated by her local gastroenterologist. She subsequently presented to our clinic and was admitted for further evaluation and possible surgical management.

Her physical exam was significant for a right-sided ileostomy with a retracted, stenosed stoma and adjacent 3-cm diameter ulceration (Figure 1). She was started on empiric intravenous corticosteroids for presumed pyoderma gangrenosum and underwent an abdominal magnetic resonance imaging enterography, which identified several areas of ileal wall thickening and enhancement concerning for active inflammation as well as multiple hypoenhancing liver lesions concerning for metastatic disease.

Adenocarcinoma was identified on biopsy of a liver lesion, but the immunostaining pattern was nonspecific to the site of origin. Ileoscopy identified focal strictures with mild inflammation and normal intervening mucosa. The center of the parastomal ulcer was biopsied and demonstrated poorly differentiated adenocarcinoma, positive for cytokeratin 7, cytokeratin 19, and polyclonal CEA and negative for cytokeratin 20, caudal-type homeobox gene 2,

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Figure 1. Ileostomy with retracted and stenosed stoma with adjacent 3-cm diameter ulceration and friability with raised border.

natural endopeptidase, and glypican 3. Serum tumor markers demonstrated a CEA of 1.6 ng/mL (normal <3.0 ng/mL) and cancer antigen 19-9 of 183 U/mL (normal <34 U/mL).

The patient underwent resection of the ileum, ileostomy, and abdominal wall with creation of a neo-end loop ileostomy. Pathology revealed poorly-differentiated, invasive adenocarcinoma extending to the stoma site (Figure 2). The background small bowel demonstrated focal transmural inflammation and minimal architectural distortion, consistent with active CD. Taken together with the overall morphology, the findings were most consistent with a small bowel primary adenocarcinoma. Multiple separate tumor nodules were present in the serosa, favoring metastasis. However, 0 out of 13 lymph nodes were involved. Postoperatively, palliative

chemotherapy was planned with 5-fluorouracil, leucovorin and oxaliplatin and bevacizumab. She currently remains off treatment for CD.

DISCUSSION

To date, there have been only 3 prior reports of primary adenocarcinoma of an ileostomy in CD (Table 1). Our case represents the longest interval, 47 years, between creation of an ileostomy to diagnosis of ileostomy adenocarcinoma in CD. A prior review of 37 patients with ileostomy adenocarcinoma by Metzger et al identified an interval greater than 20 years from ileostomy creation to diagnosis of ileostomy adenocarcinoma in greater than 70% of cases reviewed.³

Including our patient, all 4 patients reviewed had a history of Crohn's ileocolitis and underwent proctocolectomy with end-ileostomy creation. In 2 cases reported by Sherlock et al, both patients were reported to have quiescent disease from time of ileostomy creation to diagnosis of adenocarcinoma contrasted with our patient, who had several recurring flares and active ileitis prior to diagnosis of cancer.⁵ Two of 4 patients had a history of stricturing disease, 1 had penetrating disease, and 1 had oral and cutaneous manifestations of CD. All patients presented at the time of cancer diagnosis with a new peristomal lesion and inflammation at the stoma site. The differential of a stomal lesion includes Crohn's ileitis, ulcerative inflammatory reactions, pyoderma gangrenosum, granulation tissue, malignancy, and cutaneous infection.

Several mechanisms have been proposed to explain the etiology of ileostomy adenocarcinoma and its increased incidence over small bowel malignancy in the general population. Mimura et al proposed 4 differing hypotheses, including colonic metaplasia of the ileostomy, migration of colonic mucosa

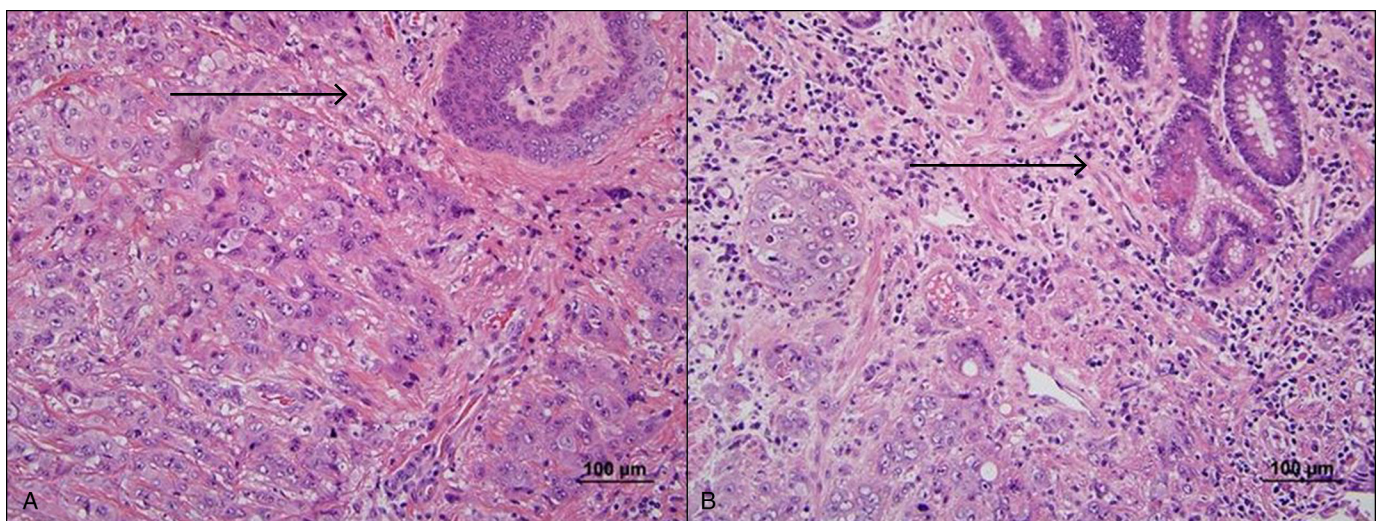


Figure 2. Primary ileostomy poorly differentiated adenocarcinoma extending to adjacent skin (A) at the stoma site and to adjacent CD (B) with pyloric metaplasia and glandular architectural distortion.

Table 1. A Review of Four Cases of Primary Adenocarcinoma of an Ileostomy in Crohn's Disease

| Author (reference) | Age (yr) | Sex | Disease Course | Surgical History | Time From Primary Surgery (yr) | Tumor Description | Metastases | Histology | Follow-Up |
|--------------------|----------|-----|---|---|--------------------------------|--|---------------------------------|---|---|
| Sherlock et al | 56 | F | Oral ulcers, pyoderma gangrenosum, remained well for 23 years after surgery | Ileocolonic resection with proctocolectomy 4 months later | 23 | 2.5-cm peristomal nodule | No | Moderately differentiated mucin secreting adenocarcinoma with high grade dysplasia | Alive at 18 months |
| Sherlock et al | 56 | M | Perirectal abscesses, anal fistulae, stricturing | Cecostomy with proctocolectomy 9 months later | 32 | 5-cm mass below ileostomy | Positive iliac nodes | Mucinous adenocarcinoma with high grade dysplasia | Died 3 years after presentation |
| Metzger et al | 66 | F | Not available | Proctocolectomy and ileostomy | 46 | 3 x 4-cm friable, granulation tissue on inferior stoma | No | Mucinous adenocarcinoma | No recurrence at 11 years, CEA levels normalized |
| Our patient | 61 | F | Stricturing disease, recurrent flares after proctocolectomy | Proctocolectomy and ileostomy | 47 | 3-cm peristomal ulceration, retracted and stenotic stomal aperture | Liver, serosa, 0/13 lymph nodes | Poorly differentiated, adenocarcinoma invading into serosal surface and extending to stoma site | Alive at 3 months, planning for palliative chemotherapy |

into the ileostomy, chronic chemical and mechanical irritation, and backwash ileitis in patients with ulcerative colitis.⁴ Our patient was found to have active ileitis with focal stricturing and is the first case report with evidence of active inflammation at time of adenocarcinoma diagnosis, suggesting that the development of her ileostomy adenocarcinoma was driven by surrounding active small bowel inflammation.

The majority of ileostomy carcinomas identified are adenocarcinoma, although squamous cell carcinoma of an ileostomy is an even more rare event that has also been reported, but not in CD.⁶ Three out of 4 patients reviewed had evidence of metaplasia or dysplasia surrounding the adenocarcinoma. This suggests that CD patients with ileostomy identified to have metaplastic or dysplastic mucosa on biopsy should undergo evaluation for a potential coexistent malignancy.

Treatment of ileostomy adenocarcinoma consists of resection of the ileostomy and surrounding abdominal wall with relocation of ileostomy. Some studies have also suggested that small bowel adenocarcinoma is sensitive to adjuvant chemotherapy regimens commonly used for treatment of colorectal cancer.⁷ The CEA level was also found to normalize after treatment in 1 case reviewed, suggesting that it could be a marker used to evaluate treatment response.³

Ileostomy adenocarcinoma in non-CD populations has a good prognosis. Metzger et al reported an 85% survival rate with surgical resection and a 15% rate of lymph node metastasis.³

In contrast, the prognosis of adenocarcinoma of the small bowel in CD has been found to be poor, with only a 20%–30% 5-year survival rate.⁸ Our patient is the first case to report liver metastases at initial presentation. One previously reported CD patient with metastatic disease lived only 3 years after diagnosis, whereas the 2 patients without metastatic disease had a similar prognosis to ileostomy adenocarcinoma in all populations.

Our understanding of progression, prognosis, and treatment of adenocarcinoma of an ileostomy in CD remains limited by the rarity of cases reported in the literature. We recommend annual physical examination of an ileostomy site in all patients and patient education to maximize early detection. Although there are no standards for optimal surveillance of ileostomies, early biopsy should be performed as part of the diagnostic evaluation for any new or persisting peristomal lesions.

DISCLOSURES

Author contributions: K. Liu reviewed the literature and wrote the manuscript. MA Prasad, A. Lo, E. Bellaguarda and S. Strong drafted and edited the manuscript. SB Hanauer revised the manuscript and is the article guarantor.

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